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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/993,366	11/21/2001	George Jackowski	2132.101	5753

7590 10/06/2005

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EXAMINER	
DAVIS, DEBORAH A	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 10/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/993,366	JACKOWSKI ET AL.	
	Examiner	Art Unit	
	Deborah A. Davis	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 39-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 39-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 12, 2005 has been entered. Currently, claims 1 and 39-46 are pending. Claims 2-38 have been canceled and claims 1, 39-40, 44-46 are currently amended.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 1 and 39-46 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial, credible or a well established utility.

Claim 1 is drawn to a biopolymer marker consisting of SEQ ID NO: 1 and a method of using. The instant claims and the specification asserts that biopolymer marker is recited to be useful in methods determining the differential expression/absence/presence of SEQ ID NO: 1 that asserts a linkage or association with insulin resistance.

Applicant has disclosed in the specification that SEQ ID NO: 1 is differentially measurable in patients with insulin resistance in comparison to samples from normal

patients (page 46, lines 4-11). Applicant's have disclosed in the remarks/arguments (page 24, paragraphs 1-3) that the marker is present in one patient with insulin resistance and absent in the other patient with insulin resistance. Applicant's have also disclosed that the marker is absent in the patients with Diabetes I and Diabetes II (see Figure I and applicant's arguments page 22). Therefore the differential expression of SEQ ID NO: 1 is not evident and the data results are ambiguous. The examiner maintains that the correlation with respect to insulin resistance is not exemplified or disclosed in the specification. With respect to page 46 of the specification that discloses markers can be differentially expressed in disease states is noted, however the SEQ I.D. that applicant recites has not been shown to be linked to insulin resistance because the marker is expressed in all normal samples and one sample of insulin resistance and not in the other patient with insulin resistance. Therefore, the teaching is ambiguous and one of ordinary skill in the art would not be able to distinguish a credible, substantial and specific utility that SEQ I.D. No. 1 is linked to insulin resistance. One of ordinary skill in the art could not distinguish if the marker is linked to insulin resistance, diabetes I or diabetes II. Although the MPEP does not require examples, however, the teaching provided must be substantial enough to enable one of ordinary skill in the art to ascertain the credibility of the evidence presented. Accordingly, the specification does not identify a substantial, credible or well-established utility for sequence consisting of SEQ ID NO: 1 and methods of use including the claimed kit consisting of SEQ ID NO: 1.

Claims 1 and 39-46 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantial,

credible or a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 39-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Although one of ordinary skill in the art can make or reproduce SEQ ID NO: 1, the specification does not have sufficient teaching on how to use the biopolymer consisting of SEQ ID NO: 1. Factors that the examiner considered in determining, whether a disclosure would require undue experimentation include 1) the predictability or lack thereof in the art, 2) the quantity of experimentation necessary, 7) the relative skill of those in the art.

Claims 1 and 39-46 are directed to a biopolymer consisting of SEQ ID NO:1 associated with insulin resistance. However, the specification does not support this assertion. The specification (in particular page 46) and the figures do not definitively

correlate a differential expression of the claimed marker consisting of SEQ ID NO:1 in insulin resistance in comparison to samples from normal patients and patients with diabetes I and II.

There is no sufficient teaching the specification that would enable one to choose SEQ ID NO:1 as notable sequences among an infinite number of possible proteins or peptides present in a patient sample. There is no correlation between the procedure for screening samples from patients suspected of having a insulin resistance or diabetes I or II.

Furthermore, Applicants have not provided any disclosure enabling the use of the biopolymer marker with regard to regulating the presence or absence of said sequence. The disclosure is equally lacking any teaching for how the identified sequence will be utilized to identify a link to insulin resistance.

Applicants have not set forth any supporting evidence that suggests that SEQ ID NO:1 is associated with insulin resistance or any other disease and the prior art teaches that disease markers are highly unpredictable and require extensive experimentation.

Tockman et al. (Cancer Research 52:2711s-2718s, 1992) teach considerations necessary for a suspected cancer biomarker (intermediate end point marker) to have efficacy and success in a clinical application. Although the reference is drawn to biomarkers for early lung cancer detection, the basic principles taught are clearly applicable to other disorders.

Tockman teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials, see abstract. Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and **if validated** (emphasis added) can be used for population screening (p. 2713s, column 1).

The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease. "This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point [marker]", see page 2714s, column 1, Biomarker Validation against Acknowledged Disease End Points section. Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials, see page 2716s, column 2, Summary section.

Tockman reiterates that the predictability of the art in regards to cancer prognosis and the estimation of life expectancies within a population with a disease or disorder are highly speculative and unpredictable.

The instant disclosure has not addressed the issues taught in the prior art as crucial to the discovery of a biopolymer marker.

The predictability or lack thereof in the art- there is no predictability based on the instant specification that the biopolymers are indicative of any disease state including insulin resistance.

The quantity of experimentation necessary- it would require undue amount of experimentation for the skilled artisan to use the biopolymers as claimed.

While it is not necessary to show working examples for every possible embodiment, there should be sufficient teachings in the specification that would suggest to the skilled artisan that the breadth of the claimed biopolymer is enabled for its use. This is not the case in the instant specification.

In view of the teachings of In re Wands, 8 USPQ2d 1400, it has been determined that the level of experimentation required to enable the breadth of the claims is undue.

Response to Arguments

5. Applicant argues that predicted residues are often shown enclosed in parentheses to separate the predicted residues from identified residues but have removed the phrase "amino acid residues 2-12" and have amended the claims to be drawn t a biopolymer marker consisting of SEQ ID NO: 1. This argument has been found to be persuasive. Therefore, the new matter rejection under 35 USC 112 is hereby withdrawn.

6. Applicant's argument that the claims have been amended to remove the term "diagnostic" and have established that the biopolymer marker consisting of SEQ ID NO: 1 is indicated as a link to insulin resistance have been considered, but not found to be persuasive for reasons set forth in the newly applied utility rejection above.

7. Applicant argues that claim 1 has been amended to specifically recite an isolated peptide consisting of SEQ ID NO:1 and does not recite that the claimed peptide is diagnostic for insulin resistance nor does it recites that SEQ ID NO: 1 is related to insulin resistance. Applicant further contends that the specification fully supports that SEQ ID NO: 1 is diagnostic of and linked to insulin resistance. Applicant asserts that the closed language "consisting of" limits the scope of SEQ ID NO:1 only to the specific peptide. This argument is noted but not found to be persuasive.

In response, although claim 1, does not recite that SEQ ID NO: 1 is linked to insulin resistance, nor does claims 44-46 which are drawn to a kit consisting of SEQ ID NO: 1, claims 39-43 are drawn to a method of determining SEQ ID NO: 1 reciting a link to insulin resistance; the specification also asserts that insulin resistance is the claimed utility for SEQ ID NO: 1. The examiner has applied a utility rejection to claims 1 and 39-46 above.

8. Applicant argues that peptides that are differentially expressed between a disease state and a normal physiological state are often determined to be associated with the disease state. Applicant further argues that the claimed biopolymer marker

peptide is identified in all of the normal samples and in one disease sample and likewise is absent in four disease samples; thus, the instant inventors link the claimed biopolymer marker peptide with insulin resistance. This argument is noted but not found to be persuasive.

In response, the examiner maintains that one of ordinary skill in the art could not ascertain a substantial, well-established or credible utility for SEQ ID NO: 1 being linked to insulin resistance, diabetes I or II, because the marker is expressed in all of the normal samples and one sample of insulin resistance and not in the other (see Figure 1). The teaching of the specification is ambiguous because it does not clearly show that SEQ ID NO: 1 is linked to insulin resistance. The examiner maintains that one of ordinary skill in the art would not be able to distinguish a credible, substantial and specific utility linked to insulin resistance. The examiner does not dispute the protocols used in identifying differentially expressed makers to identify a link to a disease state, however, the utility must be specific, credible and well established.

9. Applicant argues that the declaration under 37 CFR 1.132 filed on September 22, 2003 is sufficient to overcome the rejection of claim 1 and 39-46 based on the 112 first rejection as set forth in the last Office Action, dated December 3, 2003, because Figure 1 is not ambiguous. This argument is noted but not found to be persuasive.

In response, although a total enablement rejection was applied in the previous office action, the previous enablement rejection is hereby withdrawn on the basis of a protocol of making a peptide. However, the basic thrust of the rejection is the same.

The examiner has modified the rejection on the basis of not having a specific, well-established or substantial utility (see above utility rejection) and since utility is use, which is part of a 112 first enablement rejection, applicant is not enabled for its use.

10. Applicant arguments that the Tockman et al reference was not relevant to the instant invention because they do not teach SEQ ID NO: 1 linked to insulin resistance. This argument have been considered but not found to be persuasive.

In response, the references were cited to show the state of the art with respect to marker discovery. A rejection is proper though a reference is not prior art when it establishes the level of ordinary skill in the art at the time of the claimed invention. Ex parte Erlich, 22 USPQ 2d 1463, 1465 (Bd.Pat.App,1992). The enablement issue is whether one skilled in the art could used SEQ ID NO:1 as a link to insulin resistance without undue experimentation at the time the application was filed. The specification have not clearly set forth a link between the claimed sequence and insulin resistance, therefore undue experimentation is required and the rejection is hereby maintained.

Conclusion

11. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah A. Davis whose telephone number is (571) 272-0818. The examiner can normally be reached on 8-5 Monday thru Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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